



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/553,368	04/20/2000	Charles R. III	TTI-180DV	5076

959 7590 06/10/2002

LAHIVE & COCKFIELD
28 STATE STREET
BOSTON, MA 02109

EXAMINER

SCHNIZER, HOLLY G

ART UNIT	PAPER NUMBER
----------	--------------

1653

DATE MAILED: 06/10/2002

h

Please find below and/or attached an Office communication concerning this application or proceeding.

FILE COPY

Office Action Summary

Application No.

09/553,368

Applicant(s)

ILL ET AL.

Examiner

Holly Schnizer

Art Unit

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 March 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 40-42 and 44-71 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 40-42, 44-49, 51-56, 59, 60, 66 and 67 is/are allowed.
- 6) ☒ Claim(s) 57, 58, 61-65 and 68-71 is/are rejected.
- 7) ☒ Claim(s) 50 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 April 2000 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 09/205,817.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

Art Unit: 1653

DETAILED ACTION

Status of the Claims

The Amendment and Response filed March 14, 2002 has been entered and considered. Claim 43 has been cancelled. Claims 57-71 have been added. Therefore, Claims 40-42 and 44-71 are pending.

Declaration

The Declaration under 37 C.F.R. 1.132 by Charles R. III filed March 14, 2002 (Paper No. 10) has been entered and considered.

Drawings

As stated in the previous Office Action, the Drawings filed April 20, 2000 have been objected to by the draftsperson for reasons cited on the Form PTO-948 attached to Paper No. 8. Correction is required.

Rejections Withdrawn

The rejection of Claims 40-47 and 49-56 under 35 U.S.C. 102(a) as being anticipated by III et al. (Blood Coagulation and Fibrinolysis (Dec. 1997) 8(suppl. 2): S23-S30; ref. B7 of IDS of Paper No. 4) is withdrawn in light of the Declaration under 37 C.F.R. 1.132 by Charles R. III filed March 14, 2002 (Paper No. 10) stating that the additional authors on the references, Burns, Bartholomew, and Scuderi, provided only technical assistance, and therefore the work described therein is Applicants own work.

Art Unit: 1653

The rejection of Claims 40-47 and 49-56 under 35 U.S.C. 102(a) as being anticipated by Ill et al. (Thrombosis & Hemostasis, (July 1997) ISSN: 0340-6245; ref. B8 of IDS of Paper No. 4) is withdrawn in light of the Declaration under 37 C.F.R. 1.132 by Charles R. Ill filed March 14, 2002 (Paper No. 10) stating that the additional authors on the references, Burns, Bartholomew, and Scuderi, provided only technical assistance, and therefore the work described therein is Applicants own work.

The rejection of Claims 40 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Wolf et al. (J. Cell Biochem. (1990) Suppl. 14A, D432) (incorrectly referred to as Gould et al. in the previous Office Action) is withdrawn in light of the Amendment to Claim 40 that adds the limitation that the liver-specific promoter is the human thyroid binding globulin promoter. Applicants were correct that the examiner intended to cite Wolf et al. and was referring to abstract D432 by Wolf et al. rather than the abstract by Gould et al.

The rejection of Claims 40, 41, and 45 under 35 U.S.C. 102(e) as being anticipated by Simonet et al. (U.S. Patent No. 6,268,212) is withdrawn in light of the amendment of Claim 40 that adds the limitation that the liver-specific promoter is the human thyroid binding globulin promoter.

The rejection of Claims 40, 41, 42, 45, 47, and 49 under 35 U.S.C. 103(a) as being unpatentable over Connelly et al. (Human Gene Therapy (1996) 7: 183-195) in view of Simonet (U.S. Patent No. 6,268,212) is withdrawn in light of the amendment of Claim 40 that adds the limitation that the liver-specific promoter is the human thyroid binding globulin promoter.

Rejections Maintained

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

New Claims 57, 58, 61-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Connelly et al. (Human Gene Therapy (1996) 7: 183-195) in view of Simonet (U.S. Patent No. 6,268,212) for the same reasons as Claims 40, 41, 42, 45, 47, and 49 in the previous Office Action.

Connelly et al. teach an expression vector comprising the albumin liver specific promoter upstream of the coding sequence for the B-domain deleted factor VIII.

Art Unit: 1653

Connelly et al. also teach the placement of an intron downstream of the promoter and upstream of the coding sequence. The intron of the Apo A1 gene is placed in the leader sequence (see p. 186, Col. 1, and Fig. 1) and contains consensus splice sites. Insertion of introns into expression vectors increases the stability of mRNA transcribed from the gene.

Connelly et al. do not teach that the expression vector contains a liver specific enhancer.

Simonet teaches an expression vector comprising a liver specific promoter, such as albumin, and the liver specific enhancer, HCR (hepatocyte control region) (see Claim 1 of Simonet). Simonet et al. also teach placement of an intron downstream from the promoter and enhancer and upstream from the coding sequence (see Figure 2A wherein HCR is the enhancer, ApoE contains the promoter and intron, and IL-8 is the coding sequence). Insertion of introns into expression vectors is thought to increase stability of the mRNA transcribed from the gene.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the expression vector of Connelly et al. to include a liver specific enhancer such as the HCR enhancer taught in Simonet. Connelly et al. indicates that there is a need in the art to increase expression and liver specificity of factor VIII (see p. 184, Col. 1). Connelly et al. indicate that obtaining liver specificity at the transcriptional level could be achieved by inclusion of regulatory elements or a liver-specific promoter into the expression vector disclosed therein (p. 184, Col. 1, last 7 lines of second paragraph). Connelly et al. show that insertion of a liver specific albumin promoter

Art Unit: 1653

resulted in high level expression of the B-domain deleted Factor VIII specifically in liver cells. One of skill in the art would have looked to Simonet to improve on the expression vector of Connelly et al. since Simonet indicates that the HCR enhancer is functional with the albumin promoter (the promoter used in the Connelly et al. vector)(Col. 7, lines 26-32), the HCR enhancer can confer a significant degree of liver specific expression of a transgene and can increase the level of expression of a transgene in the liver (Col. 5, lines 42-45). Thus, it appears that the claims are unpatentable over the prior art.

New Objections/Rejections

Double Patenting

Claim 50 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 44. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). In the instant case, Claim 40 (from which Claim 44 depends) has been amended to include the limitation that the liver specific promoter is the human thyroid binding globulin promoter. Thus, the vectors of both Claims 44 and 52 now comprise the human thyroid binding globulin promoter and the alpha-1 microglobulin/bikunin enhancer and are therefore identical. Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 62, 68-71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 62 recites the limitation "the gene" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 65 recites the limitation "the gene" in line 3. There is insufficient antecedent basis for this limitation in the claim.

Claim 68 is indefinite because it is unclear whether it further limits Claim 68 from which it depends. Claim 68, ultimately dependent from Claim 57, contains the limitation that "the human thyroid binding globulin promoter and alpha-1 microglobulin/bikunin enhancer are located upstream from the coding sequence of a gene." Since proteins are expressed from coding sequences from genes, it appears that this limitation is not different from that of being located upstream from a coding sequence for a human Factor VIII protein" in Claim 57. Alternatively, if Claim 68 was intended to be broader than the claim from which it depends, then this is indefinite for not further limiting the claim as well. Claims 69-71 are rejected since they depend from an indefinite base claim and do not correct its deficiencies. Correction is required.

Art Unit: 1653

Conclusions

Claims 57, 58, 61-65, and 68-71 are rejected, Claim 50 is objected to, and Claims 40, 41, 42, 44-49, 51-56, 59-60, 66, and 67 appear to be allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Holly Schnizer whose telephone number is (703) 305-3722. The examiner can normally be reached on Mon. & Thurs., 8am-5:30pm and Tues. & Wed. 9-2:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703)

Application/Control Number: 09/553,368

Page 9

Art Unit: 1653

308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

HS

Holly Schnizer
June 6, 2002

Christopher S. F. Low
CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1800